UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,291	10/26/2001	Stephan von Horsten	20488/12 U.S.	9996

7590 06/17/2003

Mark A. Hofer, Esq.
Brown, Rudnick, Freed & Gesmer
One Financial Center
Boston, MA 02111

EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/014,291	HORSTEN ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Status of the claims

1. Claims 1, 4-6 have been amended and claims 7-13 have been added as requested in the amendment of Paper No. 6, filed on April 10, 2003.

Claims 1-13 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I in Paper No. 6 is acknowledged. The traversal is on the ground(s) that a separate search for inventions of Groups I and II is not required and, therefore, there will be no burden on the Examiner to examine two groups together. This was found to be persuasive and inventions of Groups I and II have been rejoined.

Applicant's election of species of "anxiety disorders" for conditions recited in claim 2 is acknowledged.

Claims 1-13 are under examination in the instant office action.

Specification

3. The abstract of the disclosure is objected to because it is not limited to a single paragraph. Correction is required. See MPEP § 608.01(b).

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see pages 23, 25, 28 and 31, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP §

608.01. Applicant is advised to review the entire text of the instant specification for proper use of hyperlinks.

Claim Objections

5. Claim 1 is objected to because of the following informalities: "an inhibitor to the DP IV enzyme" should be "an inhibitor of DP IV enzyme", perhaps. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3-6, 9 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 3-6, 9 and 11-12 are drawn to a method for modulating behavioral and neurological adaptive responsiveness to stress by applying to the central nervous system a therapeutically effective amount of an inhibitor of the DP IV enzyme. The instant specification fails to define any specific criteria, which clearly identify behavioral and neurological adaptive responsiveness to stress one would wish to modulate. In the absence of clear understanding what

parameters are intended to be modulated one skilled in the art would clearly not be able to practice the instant method as currently claimed.

The instant specification describes the results of administration of DPIV inhibitor using specific substrains of rats as an animal model for anxiety and stress. It appears that administration of DPIV inhibitors leads to reduction in anxiety and stress responsiveness in rats as measured in different behavioral tests (see Examples on pp. 23-33 of the instant specification). Based on these results, one would reasonably conclude that administration of DPIV inhibitors leads to certain behavioral effects generally associated with reduction in stress and anxiety in rats. However, the instant claims encompass a method for "modulating behavioral and neurological adaptive responsiveness to stress". The term "modulating" generally stands for "increasing or decreasing". The instant specification fails to provide necessary guidance regarding any effect caused by administration of DPIV inhibitors other, than reduction of responsiveness to stress and anxiety. Moreover, because "modulation" characterizes any change in measurable parameters, one would not reasonably expect that administration of a therapeutically effective amount of an inhibitor of DP IV enzyme would have an ability to provide for both effects. Thus, the instant specification fails to provide guidance on how to practice a method of administration of an inhibitor of the DP IV enzyme, which would lead to two opposite effects, such as "increase" or "decrease". It would require undue experimentation on part of a skilled artisan to discover how to practice Applicant's invention, as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1 is indefinite for recitation of an acronym, "DP IV", without providing a full name at the first appearance of the term.

9. Claim 1 is further vague and ambiguous for recitation "modulating behavioral and neurological adaptive responsiveness". The metes and bounds of this recitation cannot be determined from the claim or the instant specification. See also reasoning earlier in section 6 of the instant office action.

10. Claim 1 is also vague and indefinite for recitation "brain or central nervous system". Usually brain is defined as a part of central nervous system. Using two of these terms within a claim is confusing because it is not clear which term is controlling the limitation.

11. Claims 1 and 2 use the term "DP IV – like enzyme", emphasis added, which renders claims indefinite because the metes and bounds of the instant limitation cannot be determined from the claim or the instant specification. It is not obvious, which enzymes are to be included or excluded by the limitation "like".

12. Claim 2 is vague and indefinite for using an acronym CD26 without providing a full name at its first appearance.

13. Claim 2 is further vague and ambiguous for recitation "other substrates sharing similar properties". It is not clear and not defined in the instant specification what "other substrates" are intended by the claim.

14: Claims 3-5 and 7-8 recite the limitation "inhibitors" in claims 1 and 2. There is insufficient antecedent basis for this limitation in the claims.

15. Claims 4 and 7 are vague and ambiguous for recitation "will be present". Using future tense in the text of the claim implies future limitations, which renders the claim language indefinite.

16. Claims 6 and 10-13 recite the limitation "DP IV inhibitors" in claims 1, 2 and 4. There is insufficient antecedent basis for this limitation in the claims.

17. Claim 9 is indefinite for being dependent from indefinite claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 2, 7-8, 10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Powers et al. (WO 95/2961, 1995, Document BL, IDS of Paper No.2).

Claims 2, 7-8, 10 and 13 are directed to a method for reducing degradation of the NPY and other substrates sharing similar properties by administration of a therapeutically effective amount of an inhibitor of DPIV. Powers et al. disclose inhibitors of dipeptidyl peptidase IV and their use for administration as anti-inflammatory agents, anticoagulants, anti-tumor agents and anti-AIDS agents (see abstract, also page 19 and claims 6-8, page 37). Administration of

therapeutical amount of inhibitors of Powers et al. leads to the decrease of enzymatic activity of DPIV and, consequently, to the reduction of degradation of its natural endogenous substrate. Thus, the disclosure of Powers et al. meets the limitations of claim 2. Furthermore, inhibitors of Powers et al. are disclosed as free inhibitors (claims 1-5, page 34-37) and also in formulations "as tablets, troches, lozenges, aqueous or oily suspension, dispersible powders or granules, emulsions, hard or soft capsules or syrups or elixirs" (page 19, lines 25-27), which may be administered orally, topically or parenterally (page 19, line 22). Therefore, the disclosure of Powers et al. anticipates claims 7-8, 10 and 13.

19. Claims are rejected under 35 U.S.C. 102(b) as being anticipated by Powers et al. (WO 95/2961, 1995, Document BL, IDS of Paper No.2) in view of WO 97/40832 document (reference BE, IDS of Paper No. 2) and Lader, 1981.

Claims 1, 3-6, 9 and 11-12 are drawn to a method for modulating behavioral and neurological adaptive responsiveness to stress and therapy of anxiety disorders by applying to the central nervous system a therapeutically effective amount of an inhibitor of the DPIV enzyme. Powers et al. disclose administration of therapeutical amount of an inhibitor of DPIV for treatment purposes of inflammation and as anticoagulants, anti-tumor agents and anti-AIDS agents, as explained earlier in section 19 of the instant office action. Because the document of Powers et al. fully discloses the step of administration of DPIV inhibitors, the results of the same procedure are reasonably expected to be same. As such, the administration of DPIV inhibitors as disclosed by Powers et al. leads to reduction in stress responsiveness and anxiety. This especially true in view of art recognition of use of DPIV inhibitors to alter blood sugar levels (see WO 97/40832, document BE, IDS of Paper No. 2) and close association of anxiety and abnormal

concentration of blood glucose (see Lader, 1981, abstract and whole paper). One would reasonable expect that administration of a DPIV inhibitor to treat inflammation, AIDS and blood coagulation as disclosed by Powers et al. or to alter blood sugar level, a syndrome closely associated with anxiety, as disclosed by WO 97/40832 document would lead to therapy of anxiety and reduction of stress responsiveness, as disclosed in the instant specification.

The discovery of an inherent property of a prior art process cannot serve as a basis for patenting that process. See *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.).

Therefore, Powers et al. anticipate claims 1, 3-6 and 11-12 of the instant invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

20. Claims 1-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Demuth et al., US Patent 6,319,893, 11/20/2001, filed 08/02/1999.

Demuth et al. describe administration to the mammal a therapeutically effective amount of an inhibitor of DPIV (see abstract). Also disclosed are methods of administration (parenterally, orally), pure forms of inhibitors and in formulations with physiologically acceptable adjuvants (see column 4, lines 29-46 and claims 1-4). For specific reasoning and detailed comparison of all the claims limitations see sections 19 and 20 earlier in the instant office action. Thus, the disclosure of Demuth et al. anticipates claims 1-13 of the instant invention.

The applied reference has a common inventor, Demuth, with the instant application.

MPEP 2136.04 [R-1] Different Inventive Entity; Meaning of "By Another" states that IF THERE IS ANY DIFFERENCE IN THE INVENTIVE ENTITY, THE REFERENCE IS "BY ANOTHER". "Another" means other than applicants, In re Land, 368 F.2d 866, 151 USPQ 621 (CCPA 1966), in other words, a different inventive entity. The inventive entity is different if not all inventors are the same. The fact that the application and reference have one or more inventors in common is immaterial. Ex parte DesOrmeaux, 25 USPQ2d 2040 (Bd. Pat. App. & Inter. 1992) (The examiner made a 35 U.S.C. 102(e) rejection based on an issued U.S. patent to three inventors. The rejected application was a continuation- in-part of the issued parent with an extra inventor. The Board found that the patent was "by another" and thus could be used in a 35 U.S.C. 102(e) /103 rejection of the application.).

Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was

derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,319,893. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The instant invention is directed to a method of administration of DPIV inhibitors for reduction of degradation of DPIV substrate and therapy of anxiety and responsiveness to stress. US Patent 6,319,893 ('893 patent) fully discloses the step of administration of DPIV inhibitors for alteration of blood sugar levels. Because instant claims 2, 7-8, 10 and 13, directed to a method administration of DPIV inhibitor for reducing degradation of DPIV substrate fully encompass the claims of '893 patent, directed to a method of altering blood sugar level as a result of reduction of degradation of DPIV substrate by administration of DPIV inhibitor, the

patent claims anticipate the pending claims 2, 7-8, 10 and 13. Furthermore, because the instant invention encompasses claims directed to therapy of anxiety disorders by administration of DPIV inhibitor (see claims 1, 13-6, 9 and 11-12), and in view of *Ex parte Novitski*, as fully explained earlier in section 20 of the instant office action, the claims of '893 patent directed to administration of DPIV inhibitors to alter blood sugar levels inherently encompass therapy of anxiety disorders.

Conclusion

23. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original

signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
June 16, 2003